



Atty. Dkt. No. 071949-5408

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant: VALKIRS et al.

Title: DIAGNOSTIC MARKERS OF
STROKE AND CEREBRAL
INJURY AND METHODS OF
USE THEREOF

Appl. No.: 10/714,078

Filing Date: 11/14/2003

Examiner:

Art Unit:

CERTIFICATE OF MAILING	
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to: Commissioner for Patents, PO Box 1450, Alexandria, Virginia 22313-1450, on the date below.	
<u>DIANE GARCIA</u> (Printed Name)	
<u>Diane Garcia</u> (Signature)	
1-8-2004 (Date of Deposit)	

INFORMATION DISCLOSURE STATEMENT
UNDER 37 CFR §1.56

Commissioner for Patents
PO Box 1450
Alexandria, Virginia 22313-1450

Sir:

Applicants submit herewith on Form PTO/SB/08 a listing of the documents cited by or submitted to the U.S. PTO in corresponding application Serial Nos. 10/371,149, filed 02/20/2003 and 10/225,082, filed 08/20/2002. As provided in 37 CFR §1.98(d), copies of the documents are not being provided since they were previously submitted to the United States Patent & Trademark Office in the above-identified parent applications.

The submission of any document herewith, which is not a statutory bar, is not intended as an admission that such document constitutes prior art against the claims of the present application or that such document is considered material to patentability as defined in 37 CFR §1.56(b). Applicants do not waive any rights to take any action which would be appropriate to antedate or otherwise remove as a competent reference any document which is determined to be a *prima facie* art reference against the claims of the present application.



Atty. Dkt. No. 071949-5408

TIMING OF THE DISCLOSURE

The listed documents are being submitted in compliance with 37 CFR §1.97(b), within three (3) months of the filing date of the application.

RELEVANCE OF EACH DOCUMENT

All of the documents are in English.

Applicants respectfully request that any listed document be considered by the Examiner and be made of record in the present application and that an initialed copy of Form PTO/SB/08 be returned in accordance with MPEP §609.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 CFR §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 50-0872. Should no proper payment be enclosed herewith, as by a check being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 50-0872.

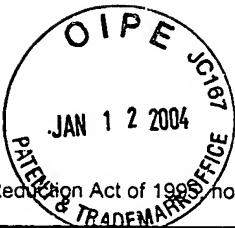
Respectfully submitted,

Date 1/8/04

By Barry Wilson

FOLEY & LARDNER
Customer Number: 30542
Telephone: (858) 847-6722
Facsimile: (858) 792-6773

Barry S. Wilson
Attorney for Applicant
Registration No. 39,431



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 1

Complete if Known

Application Number	10/ 371,149
Filing Date	02/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

Attorney Docket Number 071949-5406

U.S. PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code ² (if known)			
A1	6,235,489 B1			Jackowski et al.	May 22, 2001	
A2	6,268,223 B1			Cornell-Bell et al.	July 31, 2001	

FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No. ¹	Foreign Patent Document			Name of Patentee or Applicant of Cited Documents	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Office ³	Number ⁴	Kind Code ⁵ (if known)			
	A3	WO	00/52476 A1		Skye Pharmatech Incorporated	Sept. 8, 2000	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

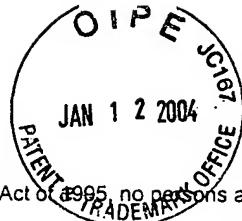
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A4	Feinberg et al., "Guidelines for the Management of Transient Ischemic Attacks." Stroke, 25(6): 1320-1335, June 1994.	
	A5	Herrmann et al., "Release of Glial tissue-specific proteins after acute stroke: A comparison analysis of serum concentrations of protein S-100B and Glial fibrillary acidic protein." Stroke, 31:2670-2677, 2000.	
	A6	Napoli et al., "C-reactive protein in ischemic stroke: An independent prognostic factor." Stroke, 32:917-924, 2001.	
	A7	Strand et al., "Brain and plasma proteins in spinal fluid as markers for brain damage and severity of stroke." Stroke: 15(1): 138-144, 1994.	
	A8	Hirashima et al., "Elevation of platelet activating factor, inflammatory cytokines, and coagulation factors in the internal jugular vein of patients with subarachnoid hemorrhage." Neurochemical Research, 22(10): 1249-1255, 1997.	

Examiner
SignatureDate
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ² See attached Kinds of U.S. Patent Documents. ³ Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴ For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵ Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶ Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



JAN 12 2004

PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

Sheet 2 of 1

Complete if Known

Application Number	10/1371,149
Filing Date	02/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	
Attorney Docket Number	071949-5406

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶

Examiner
Signature

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<p>Substitute for form 1449B/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p><i>(use as many sheets as necessary)</i></p>				<p><i>Complete if Known</i></p>	
Sheet	1	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

U.S. PATENT DOCUMENTS

FOREIGN PATENT DOCUMENTS

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

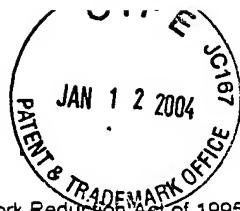
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A19	Aggarwal et al., "Evaluation of serum lipid profile and cardiac enzyme changes in cerebrovascular accidents," JIMA, 93:331-332, 1995.	

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 2 of 21

Complete if Known

Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

Attorney Docket Number 071949-5404

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A20	Akiyama et al., "Changes in serum concentrations of matrix metalloproteins, tissue inhibitors of metallo proteinases and Type IV collagen in patients with various types of glomerulonephritis," Res. Commun. In Mol. Path. and Pharm., 95(2): 115-128, 1997.	
	A21	Albrecht et al., "Detection of circulating tissue factor and factor VII in a normal population," Thrombosis and Haemostasis, 75(5): 772-7, 1996.	
	A22	Albrechtsen and Bock, "Quantification of glial fibrillary acidic protein (GFAP) in human body fluids by means of ELISA employing a monoclonal antibody." Journal of Neuroimmunology, 8:301-309, 1985.	
	A23	Austgulen et al., "Increased maternal plasma levels of soluble adhesion molecules (ICAM-1, VCAM-1, E-selectin) in preeclampsia," Eur. J. Obstet. Gynecol. Reprod. Biol., 71:53-58, 1997.	
	A24	Banks et al., "Circulating intercellular adhesion molecule-1 (ICAM-1), E-selectin and vascular cell adhesion molecule-1 (VCAM-1) in human malignancies," Br. J. Cancer, 68:122-124, 1993.	
	A25	Bates et al., "Neurotrophin-3 promotes cell death induced in cerebral ischemia, oxygen-glucose deprivation, and oxidative stress: possible involvement of oxygen free radicals," Neurobiology of Disease, 24-37, 2002.	
	A26	Benamer et al., "Comparison of the prognostic value of C-reactive protein and troponin I in patients with unstable angina pectoris," Am. J. Cardiol., 82:845-850, 1998.	
	A27	Berendes et al., "Secretion of brain natriuretic peptide in patients with aneurysmal subarachnoid hemorrhage," Lancet, 349:245-249, 1997.	
	A28	Bialik et al., "Myocyte apoptosis during acute myocardial infarction in the mouse localizes to hypoxic regions but occurs independently of p53," J.Clin.Invest., 100(6): 1363-1372, 1997.	
	A29	Biasucci et al., "Elevated levels of interleukin-6 in unstable angina," Circulation, 94:874-877, 1996.	
	A30	Biasucci et al., "Episodic activation of the coagulation system in unstable angina does not elicit an acute phase reaction," Am. J. of Cardiol., 77:85-87, 1996.	

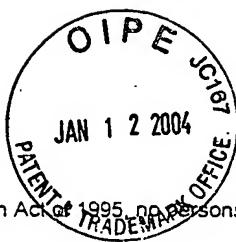
Examiner
Signature

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
Sheet 3		of 21	Attorney Docket Number 071949-5404		

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS			
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	
	A31	Biasucci et al., "Increasing levels of interleukin (IL)-1Ra and IL-6 during the first 2 days of hospitalization in unstable angina are associated with increased risk of in-hospital coronary events," Circulation, 99:2079-2084, 1999.	
	A32	Bitsch et al., "A longitudinal prospective study of soluble adhesion molecules in acute stroke," Stroke, 29:2129-2135, 198.	
	A33	Blankaert et al., "Constitutive release of metalloproteinase-9 (92-kd Type IV collagenase) by Kaposi's sarcoma cells," J. Acquir. Immune Defic. Syndr. Hum. Retrovirol., 18:203-209, 1998.	
	A34	Blann et al., "Soluble intercellular adhesion molecule-1, E-selectin, vascular cell adhesion molecule-1 and von Willebrand factor in stroke," Blood Coagul. Fibrinolysis, 10:277-284, 1999.	
	A35	Bollensen et al., "Adenylate kinase enzyme activity in cases of brain infarction," Acta Neurol. Scand., 79:53-58, 1989.	
	A36	Bonfrer et al., "The luminescence immunoassay S-100: a sensitive test to measure circulating S-100B: its prognostic value in malignant melanoma," Brit. Jour. Of Cancer, 77(12): 2210-2214, 1998.	
	A37	Bonow, "New insights into the cardiac natriuretic peptides," Circulation, 93:1946-1950, 1996.	
	A38	Bossink et al., "Plasma levels of the chemokines monocyte chemotactic proteins-1 and -2 are elevated in human sepsis," Blood, 86(10): 3841-3847, 1995.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet	4	of	21	Attorney Docket Number	071949-5404
-------	---	----	----	------------------------	-------------

Complete if Known

Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A39	Caligiuri et al., "Immune system activation follows inflammation in unstable angina: pathogenetic implications," J.Am. Coll. Cardiol., 32:1295-1304, 1998.	
	A40	Carlstedt et al., "Proinflammatory cytokines, measured in a mixed population on arrival in the emergency department, are related to mortality and severity of disease," Journal of Internal Medicaine, 242:361-365, 1997.	
	A41	Carter et al., "Platelet GP IIIa P1A and GP Ib variable number tandem repeat polymorphisms and markers of platelet activation in acute stroke," Arterioscler Thromb. Vasc. 18:1124-1131, 1998.	
	A42	Carter et al., "Purification, cloning, expression and biological characterization of an interleukin-1 receptor antagonist protein," Nature, 344:633-638, 1990.	
	A43	Catto et al., "von Willebrand factor and factor VIII: C in acute cerebrovascular disease," Thromb. Haemost., 77:1104-8, 1997.	
	A44	Curzen et al., "Can C reactive protein or troponins T and I predict outcome in patients with intractable unstable angina?" Heart, 80:23-27, 1998.	
	A45	Dangas et al., "Correlation of serum lipoprotein(a) with the angiographic and clinical presentation of coronary artery disease," Am. J. Cardiol., 83:583-585, 1999.	
	A46	Davie et al., "The coagulation cascade: initiation, maintenance and regulation," Biochemistry, 30(43): 10363-10370, 1991.	

Examiner
SignatureDate
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1996, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT <i>(use as many sheets as necessary)</i>				Complete if Known	
Sheet	5	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

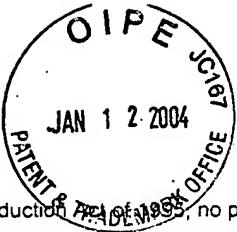
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A47	DeRose et al., "Circulating adhesion molecules in cystic fibrosis," Am. J. Respir. Crit. Care Med., 157: 1234-1239, 1998.	
	A48	Eisenberg et al., "Interleukin 1 receptor antagonist is a member of the interleukin 1 gene family: evolution of a cytokine control mechanism," Proc. Nat. Acad. Sci. USA, 88: 5232-5236, 1991.	
	A49	Emsley et al., "Crystal structure of the von Willebrand factor A1 domain and implications for the binding of platelet glycoprotein Ib," Journal of Biological Chemistry, 273(17): 10396-10401, 1998.	
	A50	Endo et al., "Elevated levels of serum and plasma metalloproteinases in patients with gastric cancer," Anticancer Research, 17:2253-2258, 1997.	
	A51	Estrada et al., "High plasma levels of endothelin-1 and atrial natriuretic peptide in patients with acute ischemic stroke," Am. J. of Hypertension, 7(12): 1085-1089, 1994.	
	A52	Fassbender et al., "Proinflammatory cytokines in serum of patients with acute cerebral ischemia: kinetics of secretion and relation to the extent of brain damage and outcome of disease," Journal of the Neurological Sciences, 122:135-139, 1994.	
	A53	Feinberg et al., "Hemostatic markers in acute ischemic stroke," Stroke, 27:1296-1300, 1996.	
	A54	Fernandes-Alnemri et al., "CPP32, a novel human apoptotic protein with homology to <i>Caenorhabditis elegans</i> cell death protein Ced-3 and mammalian interleukin-1 β -converting enzyme," Journal of Biological Chemistry, 269(49): 30761-30764, 1994.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington D.C. 20231



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031.
U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet	6	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

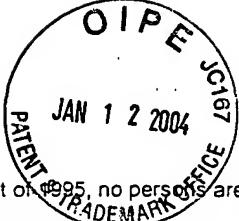
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		
	A55	Fisher et al., "Serum concentrations and peripheral secretion of the beta chemokines monocyte chemoattractant protein 1 and macrophage inflammatory protein 1 α in alcoholic liver disease," Gut, 45(3): 416-420, 1999.		
	A56	Fon et al., "Hemostatic markers in acute transient ischemic attacks," Stroke, 25(2): 282-286, 1994.		
	A57	Fujii et al., "Hemostasis in spontaneous subarachnoid hemorrhage," Neurosurgery, 37(2): 226-234, 1995.		
	A58	Fujii et al., "Serial changes of hemostasis in aneurysmal subarachnoid hemorrhage with special reference to delayed ischemic neurological deficits," J.Neurosurg., 86:594-602, 1997.		
	A59	Fujii et al., "Hemostasis in spontaneous subarachnoid hemorrhage," Neurosurgery, 37(2): 226-234, 1995.		
	A60	Gabay et al., "Interleukin-1 receptor antagonist (IL-1Ra) is an acute-phase protein," J.Clin. Invest., 99(12): 2930-2940, 1997.		
	A61	George et al., "Evidence for altered hepatic matrix degradation in genetic haemochromatosis," Gut, 42: 715-720, 1998.		
	A62	Gohji et al., "Elevation of serum levels of matrix metalloproteinase-2 and -3 as new predictors of recurrence in patients with urothelial carcinoma," Circulation, 99:608-613, 1999.		

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known
Sheet	7	of	21	Application Number Filing Date First Named Inventor Group Art Unit Examiner Name
				Attorney Docket Number 071949-5404

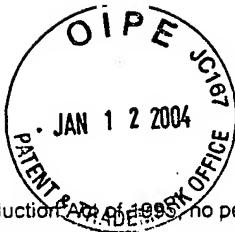
OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		
	A63	Goto et al., "Enhanced shear-induced platelet aggregation in acute myocardial infarction," Circulation, 99:608-613, 1999.		T ⁶
	A64	Guimaraes et al., "Potent constrictor actions of endothelin-1, endothelin-2, and endothelin-3 in rat isolated portal vein," Hypertension, 19(supp. II): II79-II86, 1992.		
	A65	Hanley and McNeil, "The meaning and use of the area under a receiver operating characteristic (ROC) curve," Radiology, 143:29-36, 1982.		
	A66	Hasegawa et al., "Increased levels of calbindin-D in serum and urine from patients treated by extracorporeal shock wave lithotripsy," Journal of Urology, 149:1414-1418, 1993.		
	A67	Hayasaka et al., "Elevated plasma levels of matrix metalloproteinase-9 (92-kd type IV collagenase/gelatinase B) in hepatocellular carcinoma," Hepatology, 24:1058-1062, 1996.		
	A68	Heinrich et al., "Association of variables of coagulation, fibrinolysis and acute-phase with atherosclerosis in coronary and peripheral arteries and those arteries supplying the brain," Thrombosis and Haemostasis, 73(3): 374-379, 1995.		
	A69	Hirashima et al., "Elevation of platelet activating factor, inflammatory cytokines, and coagulation factors in the internal jugular vein of patients with subarachnoid hemorrhage," Neurochem. Res., 22: 1249-1255, 1997.		
	A70	Hirashima et al., "Cerebrospinal fluid tissue factor and thrombin-antithrombin III complex as indicators of tissue injury after subarachnoid hemorrhage," Stroke, 28:1666-1670, 1997.		

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet		8	of	21	Attorney Docket Number
		071949-5404			

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A71	Hunt et al., "The amino-terminal portion of Pro-brain natriuretic peptide (pro-BNP) circulates in human plasma," Biochem. Biophys. Res. Commun., 214:1175-1183, 1995.	
	A72	Hwang et al., "Circulating adhesion molecules VCAM-1, ICAM-1 and E-selectin in carotid atherosclerosis Circulation, 96:4219-4225, 1997.	
	A73	Isgro et al., "A predictive parameter in patients with brain related complications after cardiac surgery," Eur. J. Cardiothorac. Surg., 11: 640-644, 1997.	
	A74	Jacque et al., "Myelin basic protein in CSF and blood," Arch. Neurol., 39: 557-560, 1982.	
	A75	James, T., "The variable morphological coexistence of apoptosis and necrosis in human myocardial infarction: significance for understanding its pathogenesis, clinical course, diagnosis and prognosis," Coron. Artery Dis., 9:291-307, 1998.	
	A76	Jensen et al., "Characterization of human brain S100 protein fraction: amino acid sequence of S100 β , J. Neurochem., 45:700-705, 1985.	
	A77	Johnson et al., "Activation of matrix-degrading metalloproteinases by mast cell proteases in atherosclerotic plaques," Arterioscler. Thromb. Vasc. Biol., 18:1707-1715, 1998.	
	A78	Johnsson, "Markers of cerebral ischemia after cardiac surgery," J. Cardiothorac. Vasc. Anesth., 10: 120-126, 1996	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet	9	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

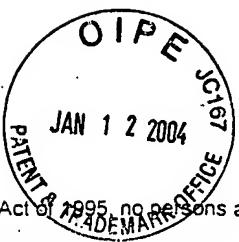
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A79	Jougasaki et al., "Adrenomedullin: potential in physiology and pathophysiology," <i>Life Sciences</i> , 66(10): 855-872, 2000.	
	A80	Kaneko et al., "Circulating levels of β -chemokines in systemis lupus erythematosus," <i>J. Rheumatol.</i> , 26: 568-573, 1999.	
	A81	Kario et al., "Silent" cerebral infarction is associated with hypercoagulability, endothelial cell damage, and high Lp(a) levels in elderly Japanese," <i>Arterioscler. Thromb. Vasc. Biol.</i> , 16: 734-741, 1996.	
	A82	Keyszer et al., "Circulating levels of matrix metalloproteinases MMP-3 and MMP-1, tissue inhibitor of metalloproteinases 1 (TIMP-1), and MMP-1/TIMP-1 complex in rheumatic disease. Correlation with clinical activity of rheumatoid arthritis versus other surrogate markers," <i>J.Rheumatol.</i> , 26:251-258, 1999.	
	A83	Keyszer et al., "Matrix metalloproteinases, but not cathepsins B, H, and L or their inhibitors in peripheral blood of patients with rheumatoid arthritis are potentially useful markers of disease activity," <i>J.Rheumatol.</i> , 57:392-398, 1998.	
	A84	Kim et al., "Involvement of oxidative stress and caspase-3 in cortical infarction after photothrombotic ischemia in mice," <i>Cereb. Blood Flow Metab.</i> , 20:1690-1701, 2000.	
	A85	Kim, "Cytokines and adhesion molecules in stroke and related diseases," <i>J.Neurol. Sci.</i> , 137:69-78, 1996.	
	A86	Kim et al., "Kidney as a major clearance organ for recombinant human interleukin-1 receptor antagonist," <i>J.Pharm. Sci.</i> , 84:575-580, 1995.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 10 of 21

Complete if Known

Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

Attorney Docket Number 071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A87	Kim et al., "Serial measurement of interleukin-6, transforming growth factor- β , and S-100 protein in patients with acute stroke," <i>Stroke</i> , 27:1553-1557, 1996.	
	A88	Koyama et al., "Determination of plasma tissue factor antigen and its clinical significance," <i>Br. J. Haematol.</i> , 87:343-347, 1994.	
	A89	Krupinski et al., "Protein kinase expression and activity in the human brain after ischaemic stroke," <i>Acta Neurobiol. Exp.</i> 58:13-21, 1998.	
	A90	Kudo et al., "Clearance and tissue distribution of recombinant human interleukin 1 β in rats," <i>Cancer Res.</i> , 50:5751-5755, 1990.	
	A91	Kuwasaki et al., "Increased plasma proadrenomedullin N-terminal 20 peptide in patients with essential hypertension," <i>Ann. Clin. Biochem.</i> , 36:622-628, 1999.	
	A92	Landi et al., "Hypercoagulability in acute stroke: prognostic significance," <i>Neurol.</i> , 37: 1667-1671, 1987.	
	A93	Laskowitz et al., "Serum markers of cerebral ischemia," <i>J. Stroke Cerebrovasc. Dis.</i> , 7:234-241, 1998	
	A94	Latini et al., "Cytokines in acute myocardial infarction: selective increase in circulating tumor necrosis factor, its soluble receptor, and interleukin-1 receptor antagonist," <i>J. Cardiovasc. Pharmacol.</i> , 23:1-6, 1994.	

Examiner
Signature

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, Respondents are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
Sheet	11	of	21	Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

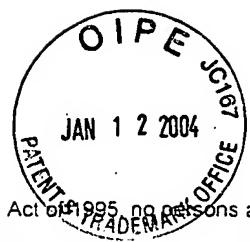
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A95	Lee and Bondy, "Insulin-like growth factors and cerebral ischemia," Ann. N.Y. Acad. Sci., 679:418-422, 1993.	
	A96	Lee et al., "Proteolytic processing of big endothelin-3 by the kell blood group protein," Blood, 94:1440-50, 1999.	
	A97	Legos et al., "Quantitative changes in interleukin proteins following focal stroke in the rat," Neurosci. Letter, 282:189-192, 2000.	
	A98	Lein et al., "Metalloproteinases (MMP-1, MMP-3) and ihre inhibitoren (TIMP) im blutplasma bei patienten mit prostatakarzinom," Urologe [A], 37:377-381, 1998.	
	A99	Li et al., "The expression of monocyte chemotactic protein (MCP-1) in human vascular endothelium <i>in vitro</i> and <i>in vivo</i> ," Mol. Cell. Biochem., 126:61-68, 1993.	
	A100	Liu et al., "Purification and characterization of an interleukin-1 β -converting enzyme family protease that activates cysteine protease P32 (CPP32)," J. Biol. Chem., 271:13371-13376, 1996.	
	A101	Liuzzo et al., "Plasma protein acute-phase response in unstable angina is not induced by ischemic injury," Circulation, 94:2373-2380, 1996.	
	A102	Long et al., "p53 and the hypoxia-induced apoptosis of cultured neonatal rat cardiac myocytes," J. Clin. Invest., 99:2635-2643, 1997.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet 12		of 21	Attorney Docket Number	071949-5404	

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A103	Love et al., "Activation of caspase-3 in permanent and transient brain ischaemia in man," Neuroreport, 11:2495-2499, 2000.	
	A104	Maiuri et al., "Serum and cerebrospinal fluid enzymes in subarachnoid haemorrhage," Neurol. Res., 11:6-8, 1989.	
	A105	Manicourt et al., "Serum levels of collagenase, stromelysin-1, and TIMP-1," Arthritis Rheum., 37:1774-1783, 1994.	
	A106	Martens et al., "Serum S-100 and neuron-specific enolase for prediction of regaining consciousness after global cerebral ischemia," Stroke, 29: 2363-2366, 1998.	
	A107	Mateo and deArtinano, "Highlights of endothelins: A review," Pharm. Res., 36(5): 339-351, 1997.	
	A108	Mathiesen et al., "Cerebrospinal fluid interleukin-1 receptor antagonist and tumor necrosis factor- α following subarachnoid," J. Neurosurg., 87:215-220, 1997.	
	A109	Matsumori et al., "Plasma levels of the monocyte chemoattractant protein-1 are elevated in patients with acute myocardial infarction," J. Mol. Cell. Cardiol., 29:419-423, 1997.	
	A110	McKeating et al., "Leukocyte adhesion molecule profiles and outcome after traumatic brain injury," Acta Neurochir. Suppl., 71:200-202, 1998.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet	13	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A111	McKeating et al., "Transcranial cytokine gradients in patients requiring intensive care after acute brain injury," Br. J. Anaesth., 78:520-523, 1997.	
	A112	Missler et al., "S-100 protein and neuron-specific enolase concentrations in blood as indicators of infarction volume and prognosis in acute ischemic stroke," Stroke, 28, 1956-1960, 1997.	
	A113	Miyata et al., "Conformational changes in the A1 domain of von Willebrand factor modulating the interaction with platelet glycoprotein Iba," Biol. Chem., 271:9046-9053, 1996.	
	A114	Montalescot et al., "Early increase of von Willebrand factor predicts adverse outcome in unstable coronary artery disease," Circulation, 98:294-299.	
	A115	Moore et al., "Collagenase expression in ovarian cancer cell lines," Gynecol. Oncol., 65:78-82, 1997.	
	A116	Mori et al., "Vasodilator effects of C-type natriuretic peptide on cerebral arterioles in rats," Eur. J. Pharmacol., 320:183-186, 1997.	
	A117	Mowla et al., "Biosynthesis and post-translational processing of the precursor to brain-derived neurotrophic factor," J. Biol. Chem., 276: 12660-12666, 2001.	
	A118	Mun-Bryce and Rosenberg, "Matrix metalloproteinases in cerebrovascular disease," J. Cereb. Blood Flow Metab., 18:1163-1172, 1998.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 14

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A119	Niebroj-Dobosz et al., "Immunochemical analysis of some proteins in cerebrospinal fluid and serum of patients with ischemic strokes." <i>Folia Neuropathol.</i> , 32: 129-137, 1994.	
	A120	Nishiyama et al., "Simultaneous elevation of the levels of circulating monocyte chemoattractant protein-1 and tissue factor in acute coronary syndromes," <i>Jpn. Circ. J.</i> , 62:710-712, 1998.	
	A121	Nishizawa et al., "Protein kinase C δ and α are involved in the development of vasospasm after subarachnoid hemorrhage," <i>Eur. J. Pharmacol.</i> , 398: 113-119, 2000.	
	A122	Ohtsuka et al., "Clinical implications of circulating soluble Fas and Fas ligand in patients with acute myocardial infarction," <i>Coron. Artery Dis.</i> , 10:221-225, 1999.	
	A123	Oltrona et al., "C-Reactive protein elevation and early outcome in patients with unstable angina pectoris," <i>Am. J. Cardiol.</i> , 80:1002-1006, 1997.	
	A124	Otsuki et al., "Circulating vascular cell adhesion molecule-1 (VCAM-1) in atherosclerotic NIDDM patients," <i>Diabetes</i> , 46:2096-2101, 1997.	
	A125	Persson et al., "S-100 protein and neuron-specific enolase in cerebrospinal fluid and serum: markers of cell damage in human central nervous system," <i>Stroke</i> , 18:911-918, 1987.	
	A126	Phanithi et al., "Mild hypothermia mitigates post-ischemic neuronal death following focal cerebral ischemia in rat brain: Immunohistochemical study of Fas, caspase-3 and TUNEL," <i>Neuropathol.</i> , 20:273-282, 2000.	

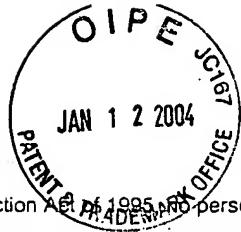
Examiner
Signature

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
Sheet 15		of 21	Attorney Docket Number		071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A127	Polin et al., "Detection of soluble E-selectin, ICAM-1, VCAM-1, and L-selectin in the cerebrospinal fluid of patients after subarachnoid hemorrhage," J. Neurosurg., 89:559-567, 1998.	
	A128	Prickett et al., "Identification of amino-terminal pro-C-type natriuretic peptide in human plasma," Biochem. Biophys. Res. Commun., 286:513-517, 2001.	
	A129	Quinn et al., "Mapping of antigenic sites in human neuron-specific enolase by expression subcloning," Clin. Chem., 40: 790-795, 1994.	
	A130	Ray et al., "Predictive factors of tumor response and prognostic factors of survival during lung cancer chemotherapy," Cancer Detect. Prev., 22: 293-304, 1998.	
	A131	Rebuzzi et al., "Incremental prognostic value of serum levels of troponin T and C-reactive protein on admission in patients with unstable angina pectoris," Am. J. Cardiol., 82:715-719, 1998.	
	A132	Robey et al., "Binding of C-reactive protein to chromatin and nucleosome core particles," J. Biol. Chem., 259:7311-7316, 1984.	
	A133	Romanic et al., "Matrix metalloproteinase expression increases after cerebral focal ischemia in rats," Stroke, 29:1020-1030, 1998.	
	A134	Rosenberg, "Matrix metalloproteinases in brain injury," J. Neurotrauma, 12:833-842, 1995.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO				Complete if Known	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
Sheet 16		of 21	Attorney Docket Number 071949-5404		

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A135	Rubattu et al., "The gene encoding atrial natriuretic peptide and the risk of human stroke," Circulation, 100:1722-1726, 1999.	
	A136	Rucinski et al., "Clearance of human platelet factor 4 by liver and kidney: its alteration by heparin," Am. J. Physiol., 251: H800-H807, 1986.	
	A137	Saraste A., "Morphologic criteria and detection of apoptosis," Herz., 24:189-195, 1999.	
	A138	Schabitz et al., "Intraventricular brain-derived neurotropic factor reduces infarct size after focal cerebral ischemia in rats," J.Cereb. Blood Flow Metab., 14: 500-506, 1997.	
	A139	Schaller et al., "Elevated levels of head activator in human brain tumors and in serum of patients with brain and other neurally derived tumors," J.Neuro-Oncol., 6:251-258, 1988.	
	A140	Schwab et al., "Plasma insulin-like growth factor I and IGF binding protein 3 levels in patients with acute cerebral ischemic injury," Stroke, 28:1744-1748, 1997.	
	A141	Seki et al., "Sustained activation of blood coagulation in patients with cerebral thrombosis," A. J. Hematol., 50: 155-160, 1995.	
	A142	Seki et al., "Plasma levels of thrombomodulin and lipoprotein (a) in patients with cerebral thrombosis," Blood Coagul. Fibrinolysis, 8:391-396, 1997.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 17 of 21

Complete if Known

Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

Attorney Docket Number 071949-5404

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A143	Shyu et al., "Serum levels of intercellular adhesion molecule-1 and E-selectin in patients with acute ischaemic stroke," J. Neurol., 244:90-93, 1997.	
	A144	Sixma et al., "Von Willebrand factor and the blood vessel wall," Mayo Clin. Proc., 66:628-633, 1991.	
	A145	Skogseid et al., "Increased serum creatine kinase BB and neuron specific enolase following head injury indicates brain damage," Acta Neurochir (Wein), 115: 106-111, 1992.	
	A146	Sorbi et al., "Elevated levels of 92-kd type IV collagenase (Matrix metalloproteinase 9) in giant cell arteritis," Arthritis Rheum., 39:1747-1753, 1996	
	A147	Steiner et al., "Increased levels of soluble adhesion molecules in Type 2 (Non-insulin dependent) diabetes mellitus are independent of glycaemic control," Thromb. Haemost., 72:979-984, 1994.	
	A148	Stockman et al., "Secondary structure and topology of interleukin-1 receptor antagonist protein determined by heteronuclear three-dimensional NMR spectroscopy," Biochemistry, 31:5237-5245, 1992.	
	A149	Stroemer et al., "Cortical protection by localized striatal injection of IL-1ra following cerebral ischemia in the rat," J. Cereb. Blood Flow Metab., 17:597-604, 1997.	
	A150	Suga et al., "Clinical significance of MCP-1 levels in BALF and serum in patients with interstitial lung diseases," Eur. Respir. J., 14:376-382, 1999.	

Examiner
Signature

Date
Considered

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents; the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO

INFORMATION DISCLOSURE
STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet

18

of

21

Complete if Known

Application Number	10/225,082
Filing Date	08/20/2002
First Named Inventor	Gunars E. Valkirs
Group Art Unit	1632
Examiner Name	

Attorney Docket Number 071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

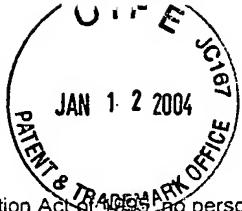
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A151	Sviri et al., "Brain natriuretic peptide and cerebral vasospasm in subarachnoid hemorrhage: Clinical and TCD correlations," Stroke, 31:118-122, 2000.	
	A152	Switalska et al., "Radioimmunoassay of human platelet thrombospondin: different patterns of thrombospondin and β -thromboglobulin antigen secretion and clearance from the circulation," J. Lab. Clin. Med., 106: 690-700, 1985.	
	A153	Takahashi et al., "Tissue factor in plasma of patients with disseminated intravascular coagulation," Am. J. Hematol., 46:333-337, 1994.	
	A154	Takano et al., "Markers of a hypercoagulable state following acute ischemic stroke," Stroke, 23:194-198, 1992.	
	A155	Tateyama et al., "Concentrations and molecular forms of human brain natriuretic peptide in plasma," Biochem. Biophys. Res. Commun., 185:760-7, 1992.	
	A156	Teitz Textbook of Clinical Chemistry, 2 nd edition, Carl Burtis and Edawrd Ashwood eds. Philadelphia: W.B.Saunders and Company, p. 496.	
	A157	Thomas et al., "Serum myelin basic protein, clinical responsiveness, and outcome of severe head injury," Acta Neurochir. Suppl., 28: 93-95, 1979.	
	A158	Tohgi et al., "Coagulation-fibrinolysis abnormalities in acute and chronic phases of cerebral thrombosis and embolism," Stroke, 21: 1663-1667, 1990.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet	19	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A159	Tomida et al., "Plasma concentrations of brain natriuretic peptide in patients with subarachnoid hemorrhage," Stroke, 29:1584-1587, 1998.	
	A160	Tousoulis et al., "Von Willebrand factor in patients evolving Q-wave versus non-Q-wave acute myocardial infarction," Int. J. Cardiol., 56:259-262, 1996.	
	A161	Trotter et al., "Immunoreactive myelin proteolipid protein-like activity in cerebrospinal fluid and serum of neurologically impaired patients," Ann. Neurol., 14: 554-558, 1983.	
	A162	Uchiyama et al., "Alterations of platelet, coagulation, and fibrinolysis markers in patients with acute ischemic stroke," Semin. Thromb. Hemost., 23: 535-541, 1997.	
	A163	Usui et al., "β-enolase in blood plasma during open heart surgery," J. Neurol., 123:134-139, 1994.	
	A164	Wada et al., "Poor outcome in disseminated intravascular coagulation or thrombotic thrombocytopenic purpura patients with severe vascular endothelial cell injuries," Am. J. Hematol., 58:189-194, 1998.	
	A165	Wang et al., "Monocyte chemoattractant protein-1 messenger RNA expression in rat ischemic cortex," Stroke, 26:661-665, 1995.	
	A166	Wijdicks et al., "Natriuretic peptide system and endothelin in aneurysmal subarachnoid hemorrhage," J. Neurosurg., 87:275-280, 1997.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

<p>Substitute for form 1449B/PTO</p> <p>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</p> <p>(use as many sheets as necessary)</p>				Complete if Known	
Sheet	20	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER PRIOR ART – NON PATENT LITERATURE DOCUMENTS

Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.	T ⁶
	A167	Wilkins et al., "The natriuretic-peptide family," Lancet, 349:1307-1310, 1997.	
	A168	Winnikes et al., "Head activator as a potential serum marker for brain tumor analysis," Eur. J. Cancer, 28:421-424, 1992.	
	A169	Woertgen et al., "Comparison of serial S-100 and NSE serum measurements after severe head injury," Acta Neurochir (Wien), 139: 1161-1165, 1997.	
	A170	Yamagami et al., "Differential production of MCP-1 and cytokine-induced neutrophil chemoattractant in the ischemic brain after transient focal ischemia in rats," J. Leukoc. Biol., 65:744-749, 1999.	
	A171	Yamazaki et al., "Alterations of haemostatic markers in various subtypes and phases of stroke," Blood Coagul., Fibrinolysis, 4:707-712, 1993.	
	A172	Yang et al., "Overexpression of interleukin-1 receptor antagonist in the mouse brain reduces ischemic brain injury," Brain Res. 751: 181-188, 1997.	
	A173	Yap et al., "Contraction to big endothelin-1, big endothelin-2 and big endothelin-3, and endothelin-converting enzyme inhibition in human isolated bronchi," Br. J. Pharmacol., 129:170-7, 2000.	
	A174	Yazdani et al., "Percutaneous interventions after the hemostatic profile of patients with unstable versus stable angina," J. Am. Coll. Cardiol., 30:1284-1287, 1997.	

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST.3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.



PTO/SB/08 (08-00)

Approved for use through 10/31/2002. OMB 0651-0031

U.S. Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449B/PTO INFORMATION DISCLOSURE STATEMENT BY APPLICANT (use as many sheets as necessary)				Complete if Known	
Sheet	21	of	21	Application Number	10/225,082
				Filing Date	08/20/2002
				First Named Inventor	Gunars E. Valkirs
				Group Art Unit	1632
				Examiner Name	
				Attorney Docket Number	071949-5404

OTHER-PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No. ¹	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.) date, page(s), volume-issue number(s), publisher, city and/or country where published.		
	A175	Yoneda et al., "Identification of a novel adenylyl kinase system in the brain: Cloning of the fourth adenylyl kinase," Mol. Brain Res., 62: 187-195, 1998.		T ⁶
	A176	Yoshimura et al., "Human monocyte chemoattractant protein-1 (MCP-1)," FEBS Lett., 244:487-493, 1989.		
	A177	Yoshitomi et al., "Plasma levels of adrenomedullin in patients with acute myocardial infarction," Clin. Sci. 94:135-9, 1998		
	A178	Zucker et al., "Increased serum stromelysin-1 levels in systemic lupus erythematosus: lack of correlation with disease activity," J.Rheumatol., 26:78-80, 1999.		

Examiner Signature	Date Considered
--------------------	-----------------

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

¹ Unique citation designation number. ²See attached Kinds of U.S. Patent Documents. ³Enter Office that issued the document, by the two-letter code (WIPO Standard ST. 3). ⁴For Japanese patent documents, the indication of the year of the reign of the Emperor must precede the serial number of the patent document. ⁵Kind of document by the appropriate symbols as indicated on the document under WIPO Standard ST. 16 if possible. ⁶Applicant is to place a check mark here if English language Translation is attached.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, Washington, D.C. 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Assistant Commissioner for Patents, Washington, D.C. 20231.